3. AIM AND OBJECTIVES

3.1 Aim

Pharmacological Screening and Evaluation of Novel Chemical Entities in Cardiometabolic Disorders.

3.2 Objectives for designed multitargeted ligands in hypertension and cardiometabolic disorders

- To develop structure activity relationships, molecular dynamics and docking simulation of potent NCEs with α_1 and AT_1 receptors.
- Pharmacological screening and evaluation of novel dual receptor antagonists by functional antagonism assay on rat abdominal aorta (pA_2 value determination).
- Docking studies of compound **(18)** and **(24)** with selected targets (DPP4 and PPARγ) for cardiometabolic disorder.
- To predict and evaluate ADMET properties of compound **(18)** and **(24)**.
- To study the toxicity of compound **(18)** and **(24)** as per the OECD guidelines.
- Evaluation of compound **(18)** and **(24)** in unilateral nephrectomy (UNX) and DOCA salt induced hypertension in rats.
- Evaluation of compound **(18)** and **(24)** in L-NAME induced hypertension in rats.
- Evaluation of compound **(18)** and **(24)** in 20 % fructose induced cardiometabolic disorder in rats.

3.3 Objectives for novel Factor Xa (FXa) inhibitors for anticoagulant and antithrombotic activity

- Pharmacological screening of NCEs for Factor Xa inhibition by human Factor Xa enzyme inhibition assay.
- Development of structure activity relationships and molecular docking of selected NCEs.
- To assess the effect of compounds **(14)** and **(50)** on intrinsic and extrinsic pathway of coagulation by prothrombin time (PT) and activated partial thromboplastin (aPTT) time measurement.
- To study the specificity of compounds **(14)** and **(50)** by human thrombin enzyme inhibition assay.

- To predict and evaluate physicochemical and ADMET properties of compound **(14)** and **(50)**.
- To study the toxicity of compounds **(14)** and **(50)** by OECD guidelines.
- To study the efficacy of compounds **(14)** and **(50)** in ferric chloride ($FeCl_3$) and arteriovenous shunt (AV shunt) induced thrombosis.